Virginia Department of Health
Anthrax: Guidance for Health Care Providers
Key Medical and Public Health Interventions After Identification of Suspected Case

1. Clinical Manifestations

A. Cutaneous Anthrax

Incubation period: Usually 1-7 days. Range is 1-12 days
Symptoms: Cutaneous anthrax occurs after direct skin contact with anthrax spores or bacilli. The skin infection begins as a small papule or vesicle that ulcerates with central necrosis and drying. Painless, localized nonpitting edema surrounds the ulcerated area, which progresses to a dark, leathery eschar. Extensive nonpitting edema, regional lymphadenopathy, lymphangitis, fever, and malaise may be present. Lesions tend to occur on exposed areas of body (e.g., face, hands, arms, neck).

B. Gastrointestinal Anthrax

Incubation period: Usually 2-5 days. Range is 1-7 days.
Symptoms: Gastrointestinal anthrax follows the consumption of raw or undercooked contaminated meat; it is associated with severe abdominal distress followed by fever and severe signs of septicemia. The oral-pharyngeal form results in lesions at the base of the tongue, sore throat, dysphagia, fever, bilateral neck swelling (caused by regional lymphadenopathy), edema, and sepsis. The abdominal form is characterized by primary intestinal lesions in the terminal ileum or cecum, presenting initially with nausea or vomiting, loss of appetite, and fever, progressing rapidly to bloody diarrhea and sepsis.

C. Inhalational Anthrax

Incubation period: Range is 2-60 days or longer; (2001 outbreak, Range 4 to 6 days)
Symptoms: Inhalation anthrax occurs after the inspiration of as few as 1-3 spores. The first stage of illness is characterized by a nonspecific prodrome of malaise, myalgias, fever, headache, nonproductive cough, nausea, abdominal pain. Some patients have brief period of apparent recovery while others progress to second stage directly. The second stage of illness develops abruptly with sudden fever, dyspnea, diaphoresis and shock, stridor in some cases with massive lymphadenopathy and widening of the mediastinum on X-ray. Cyanosis and hypotension progress rapidly to death in some patients.

2. Infection Control

Transmission from person-to-person is extremely rare. Isolation of patients is not indicated. Prophylaxis for patient contacts is not necessary unless the contacts were exposed to the same source of anthrax as the case.

Standard precautions should be followed for hospitalized patients with cutaneous, gastrointestinal or inhalational anthrax. Concurrent disinfection of articles soiled with discharge from lesions should occur. A solution of 1 part household bleach to 9 parts water (0.5% sodium hypochlorite solution) should be used. Hydrogen peroxide, paracetic acid, or glutaraldehyde may be considered as alternatives.

3. Handling Laboratory Specimens

Laboratory personnel should be alerted when anthrax is suspected to ensure safe specimen processing. Presumptive identification criteria in Level A laboratories include:

A. Direct smears from clinical samples (e.g. blood, cerebrospinal fluid, or skin lesion): Gram-positive rods.
B. Gram-stain from growth on sheep blood agar or equivalent media: Large Gram-positive rods (may stain Gram-variable).
C. Rapid, aerobic growth, and tenacious colonies on sheep blood agar.
D. Catalase positive
E. Non-motile
F. Nonhemolytic on sheep blood agar, ground-glass appearance of colonies

While hemolysis, Gram stain morphology, or motility can be used for rule out when the result provides clear evidence that the isolate is not *B. anthracis* (e.g. a clearly visible zone of beta hemolysis), a combination of two Level A tests is recommended for rule out.

The Division of Consolidated Laboratory Services (DCLS) and the Virginia Department of Health should be consulted if *B. anthracis* is suspected. The DCLS Emergency Services Officer can be reached 24 hours a day/7 days a week at (804) 418-9923. Sample collection instructions are shown in the table below.

Table 1. Sample Collection for Suspected Anthrax

Samples	*Amount*	*Type of Anthrax*	*Instructions*
Vesicle or Eschar	2 dry cotton swabs; punch biopsy if patient on antibiotics	Cutaneous	Send swabs dry in sterile container (or commercial collection device with ampule not crushed) at room temperature; Send punch biopsy in sterile container.
Blood	10 cc	Inhalational; Late Gastrointestinal	Collect in isolator tube or aerobic blood culture bottle. Store at room temperature. If in isolator tube, transport to lab within 16 hours.
Cerebrospinal Fluid	5-10 cc	Collect if meningeal signs are present	Place in sterile tube. Refrigerate.
Sputum	Non induced	Inhalational	Collect only if respiratory symptoms and sputum being produced. Send in sterile container. Refrigerate.
Stool	5-10 grams	Gastrointestinal	Place in unpreserved, sterile container. Refrigerate.

Additional laboratory guidance is available in the CDC publication *Level A Laboratory Procedures for Identification of Bacillus anthracis*, available at: http://www.bt.cdc.gov/agent/anthrax/lab-testing/index.asp

4. Diagnosis

Table 2 lists the epidemiology, diagnostic tests, microbiology, and pathology for a diagnosis of inhalational anthrax infection.

Table 2. Diagnosis of Inhalational Anthrax Infection

Category	Findings
Epidemiology	Sudden appearance of case(s) of acute febrile illness with fulminant course and death or acute febrile illness in persons identified as being at risk following a specific attack
Diagnostic Tests	Chest radiograph: widened mediastinum, infiltrates, pleural effusion Chest computed tomographic scan: hyperdense hilar and mediastinal nodes, mediastinal edema, infiltrates, pleural effusion Thoracentesis: hemorrhagic pleural effusion
Microbiology	Peripheral blood smear: Gram-positive bacilli on blood smear Blood culture growth of large Gram-positive bacilli with preliminary identification of *Bacillus* species
Pathology	Hemorrhagic mediastinitis, hemorrhagic thoracic lymphadenitis, hemorrhagic meningitis, DFA stain of infected tissues

5. Prophylaxis and Treatment

Table 3. Anthrax Recommendations for Treatment and Prophylaxis of Patients[1]

Total regimen duration should be 60 days[2]		
Treatment		Prophylaxis *May also be used when standard IV treatment is not available.*
Inhalational or Gastrointestinal Anthrax[3,4,13]	Cutaneous Anthrax[5,6,7]	
Adults (including pregnant women[8] and immunosuppressed)[9]		
Treat with IV therapy initially[10]: Ciprofloxacin, 400 mg IV[11] every 12 h **or** Doxycycline[8,12], 100 mg IV every 12 h **and** 1 or 2 additional antimicrobials[13] Switch to oral therapy when clinically appropriate: Ciprofloxacin, 500 mg PO every 12 h **or** Doxycycline, 100 mg PO every 12 h	Ciprofloxacin, 500 mg PO every 12 h **or** Doxycycline[8], 100 mg PO every 12 h **or** Alternative therapy if susceptible strain: Amoxicillin[14,15], 500 mg PO every 8 h	Ciprofloxacin, 500 mg PO every 12 h **or** Doxycycline[8], 100 mg PO every 12 h **or** Alternative therapy if susceptible strain: Amoxicillin[14,15], 500 mg PO every 8 h
Children (including immunosuppressed)		
Treat with IV therapy initially[10]: Ciprofloxacin, 10-15mg/kg IV[11] every 12 h **or** Doxycycline[12,16], 2.2 mg/kg IV every 12 h (not to exceed 100 mg/dose) **and** 1-2 additional antimicrobials[13] Switch to oral therapy when clinically appropriate: Ciprofloxacin, 10-15 mg/kg PO every 12 h (not to exceed 1 g/day) **or** Doxycycline[16], 2.2 mg/kg PO every 12 h (not to exceed 100 mg/dose)	Ciprofloxacin, 10-15mg/kg PO every 12 h (not to exceed 1 g/day) **or** Doxycycline[12,16], 2.2 mg/kg PO every 12 h (not to exceed 100 mg/dose) Alternative therapy if susceptible strain: Amoxicillin[14], ≥20kg: 500 mg PO every 8 h; <20kg: 80 mg/kg/day divided every 8 h PO (not to exceed 500 mg/dose)	Ciprofloxacin, 10-15 mg/kg PO every 12 hours (not to exceed 1 g/day) **or** Doxycycline[12,16], 2.2 mg/kg PO every 12 h (not to exceed 100 mg/dose) Alternative therapy if susceptible strain: Amoxicillin[14], ≥20kg: 500 mg PO every 8 h; <20kg: 40 mg/kg/day PO divided every 8 h (not to exceed 500 mg/dose)

NOTE: 2.2 mg/ kg refers to the amount of "two and two-tenths milligrams per kilogram" (iterated for dose clarification)

Abbreviations: IV=intravenously; PO=orally

Footnotes to Table 3:

[1] These treatment recommendations were made during US 2001 anthrax outbreak. In other situations, antimicrobial susceptibility testing should be used to guide therapy decisions.

[2] Previous guidelines have suggested treating cutaneous anthrax for 7-10 days, but 60 days is recommended for bioterrorism attacks, given the likelihood of exposure to aerosolized *B. anthracis*.

[3] Ciprofloxacin or doxycycline should be considered an essential part of first-line therapy for inhalational anthrax.

[4] Steroids may be considered an adjunct therapy for patients with severe edema (Doust 1968) and for meningitis based on experience with bacterial meningitis of other etiologies.

[5] Cutaneous anthrax cases with signs of systemic involvement, extensive edema, or lesions on the head or neck require intravenous therapy, and a multidrug approach is recommended (see Inhalational and Gastrointestinal Anthrax)

[6] Treatment of cutaneous anthrax does not prevent the evolution of the skin lesions; however, it usually will prevent progression to systemic disease.

[7] Ciprofloxacin or doxycycline should be considered first-line therapy. Amoxicillin is an option for completion of therapy after clinical improvement. Oral amoxicillin dose is based on need to achieve appropriate minimum inhibitory concentration.

[8] Although tetracyclines are not recommended for pregnant women, their use may be indicated for life-threatening illness. Adverse effects on developing teeth and bones are dose-related; therefore, doxycycline might be used for a short time (7-14 days) before 6 months of gestation.

[9] American Academy of Pediatrics considers ciprofloxacin and tetracyclines to usually be compatible with breastfeeding because the amount of either drug absorbed by infants is small, but little is know about the safety of long-term use. Therefore, amoxicillin may be considered an alternative for breastfeeding mothers if the isolate causing exposure is known to be susceptible to penicillin. Alternatively, mothers could consider expressing and discarding breast milk during therapy with ciprofloxacin or doxycycline and resuming breastfeeding after therapy is complete.

[10] Initial therapy may be altered based on clinical course of patient;' one or two antimicrobial agents (eg, ciprofloxacin or doxycycline) may be adequate as patient improves.

[11] If intravenous ciprofloxacin is not available, oral ciprofloxacin may be acceptable because it is rapidly and well absorbed from gastrointestinal tract with no substantial loss by first-pass metabolism. Maximum serum concentrations are attained 1-2 hours after oral doing but may not be achieved if vomiting or ileus is present.

[12] If meningitis is suspected, doxycycline may be less optimal because of poor central nervous system penetration.

[13] Other agents with in vitro activity include tetracycline, linezolid, macrolides, aminoglycosides, and cefazolin. *B anthracis* strains are naturally resistant to sulfamethoxazole, trimethoprim, cefuroxime, cefotaxime sodium, aztreonam, and ceftazidime. Because of concerns of constitutive and inducible beta-lactamases in *Bacillus anthracis* isolates, penicillin and ampicillin should not be used alone. Consultation with an infectious disease specialist is advised.

[14] Amoxicillin is not approved by the FDA for postexposure prophylaxis or treatment of anthrax; however, CDC indicated that it could be used for pregnant women or children for postexposure prophylaxis if the isolate is determined to be susceptible.

[15] Amoxicillin is suitable for postexposure prophylaxis only after 10-14 days of fluoroquinolones or Doxycycline treatment and then only if there are contraindications to these 2 classes of medications (e.g., pregnancy, lactating mother, age < 18 years, or intolerance of other antibiotics).

[16] The American Academy of Pediatrics recommends treatment of young children with tetracyclines for serious infections (eg, Rocky Mountain Spotted Fever).

6. Post-Exposure Prophylaxis

Post-exposure prophylaxis decisions should be made considering the epidemiological circumstances of release of *B. anthracis*. Ongoing case monitoring would be needed to define high-risk groups, to direct follow-up, and to guide the addition or deletion of groups requiring post-exposure prophylaxis. Refer to Table 3 for recommended medication doses.

7. Vaccination

The Advisory Committee on Immunization Practices currently recommends the anthrax vaccine only for: 1. People who work with anthrax in a laboratory; 2. People who work with animal hides or furs imported from high-risk areas; 3. People who will have repeated exposures to anthrax spores (e.g., workers investigating areas contaminated from a bioterrorist attack); 4. People who handle animal products in high-risk areas (e.g., veterinarians who travel to work in countries where anthrax incidence is higher); and 5. Military personnel who work in areas where anthrax could be used as a bioterrorism weapon. The vaccine is not currently recommended for others.

8. Decontamination

The greatest risk to humans exposed to aerosolized anthrax occurs during primary aerosolization (the period when spores are first made airborne). Following this period, spores may settle on surfaces, possibly in high concentrations. The risk that spores might pose through resuspension into the air is uncertain and is likely dependent on many variables including: quantity of spores on a surface; the physical characteristics of the powder used in the attack; the type of surface; the nature of the human or mechanical activity that occurs in the affected area and host factors.

Decisions about methods for decontamination following an anthrax attack should follow full expert analysis of the contaminated environment and the anthrax weapon used in the attack and should be made in consultation with experts on environmental remediation.

9. Postmortem Practices

If anthrax is suspected as a cause of death, the regional office of the state medical examiner should be notified immediately. Serious consideration should be given to cremation. If autopsies are performed, instruments and materials used during the process should be autoclaved or incinerated.

10. Public Health Measures

A. Suspected cases should be reported immediately to hospital epidemiology/infection control, who in turn should notify laboratory personnel, other medical care providers and public health. Public health officials should be notified by the most rapid means available, as soon as possible and no later than 24 hours after a suspected case is identified.
B. Arrange for laboratory testing by consulting with public health or the DCLS at 804-418-9923 (24 hour/7 day).
C. Designated public health authority should begin an epidemiologic investigation immediately.

References
Centers for Disease Control and Prevention, http://www.bt.cdc.gov

Inglesby TV; O'Toole T; Henderson DA, et al. Anthrax as a Biological Weapon: Updated Recommendations for Management. *JAMA*. 2002;287(17):2236-2252.